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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,848	01/23/2006	Tatsuo Hoshino	21415 US C038435/0185665	2032
7590 Stephen M Haracz Bryan Cave 1290 Avenue of the Americas New York, NY 10104			EXAMINER LONG, SCOTT	
			ART UNIT 1633	PAPER NUMBER
			MAIL DATE 04/28/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/528,848	Applicant(s) HOSHINO ET AL.	
	Examiner Scott D. Long	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/23/2005</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/8/2008 has been entered.

Claim Status

Claim 1 is amended. Claims 2-7 and 9-10 are cancelled. Claims 1 and 8 are under current examination.

Priority

This application claims benefit as a 371 of PCT/EPO3110574 (filed 09/23/2003). This application also claims benefit from EUROPEAN PATENT application 02021 599.2 (filed 09/27/2002). The instant application has been granted the benefit date, 27 September 2002, from the European application 02021 599.2.

Response to Arguments - Claim Rejections 35 USC § 112

Response to Arguments - 35 USC 112, second paragraph

Applicant's arguments, see pages 5-6 and Claim amendments, filed 8 February 2008, with respect to claim 6 have been fully considered, and are persuasive.

The applicant has cancelled claim 6. Therefore, this rejection is moot.

Therefore the examiner hereby withdraws the rejection of claim 6 under 35 USC 112, second paragraph.

Response to Arguments - 35 USC 112, first paragraph

Applicant's arguments, see pages 7-8 and Claim amendments, filed 8 February 2008, with respect to claim 3 have been fully considered, and are persuasive.

The applicant has cancelled claim 3. Therefore, this rejection is moot.

Therefore the examiner hereby withdraws the rejection of claim 3 under 35 USC 112, first paragraph.

Response to Arguments - Claim Rejections 35 USC § 103

Applicant's arguments, see pages 7-29 and Claim amendments, filed 8 February 2008, with respect to claims 1-3, 6 and 8-10 have been fully considered, and are persuasive.

The applicant has cancelled claims 2-7 and 9-10. Therefore, the rejection of these claims is moot.

The applicant has introduced new claim limitations, not previously included in claim 1. Claim 8 is dependent from claim 1. Accordingly, the examiner hereby withdraws the rejection of claims 1 and 8

Therefore the examiner hereby withdraws the prior art rejections of claims 1-3, 6 and 8-10 under 35 USC 103(a), second paragraph.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cunningham et al. (US-5,744,341, 28 Apr 1998) in view of Anazawa et al. (WO02/00898, published 3 Jan 2002) and further in view of Van Ooyen et al. (US-5,840,528, published 24 Nov 1998).

Claim 1 is directed to A process for producing zeaxanthin and β -cryptoxanthin which comprises cultivating a recombinant *Xanthophyllomyces dendrohous* (*Phaffia rhodozyma*) ATCC96815 which expresses a β -carotene hydroxylase gene that is originated from *Flavobacterium* sp. R1534 WT(ATCC21588) or *Erwinia herbicola* ATCC39368 in an aqueous nutrient medium under aerobic conditions, and isolating the resulting carotenoids from the cells of said recombinant microorganism or from the cultured broth, wherein the β -carotene hydroxylase gene is expressed in the recombinant *Xanthophyllomyces dendrohous* using an expression vector containing control sequences of glyceraldehyde-3-dehydrogenase gene.

Claim 8 is directed to the process according to claim 1, wherein the cultivation is carried out at pH range from 5 to 7 and at a temperature range from 18 to 22°C for 48 to 350 hours.

Cunningham et al. teach "Host systems according to the present invention can comprise any organism that already produces carotenoids or which has been genetically modified to produce carotenoids....Organisms which already produce carotenoids include...yeasts, fungi....Transformation of these hosts with vectors according to the present invention can be done using standard techniques" (col.6, lines 37-46). Cunningham et al. teach, "Suitable vectors...comprise a eukaryotic gene

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encoding an enzyme involved in carotenoid biosynthesis or metabolism and a suitable promoter for the host ” (col.6, lines 19-22). Cunningham et al. teach “The present invention also related to novel enzymes which can transform known carotenoids into novel or rare products....For example,...the gene encoding *A. thaliana* β -carotene hydroxylase...the resulting enzyme catalyzed the formation of β -cryptoxanthin as a major product and zeaxanthin as a minor product.” (col.5, lines 8-38). Cunningham et al. teach a plasmid PAC-ZETA containing β -carotene hydroxylase (CrtZ) gene from *Erwinia herbicola* (col.9, lines 11-12).

Cunningham et al. do not teach the accession number of the *Erwinia herbicola* from which the β -carotene hydroxylase gene was cloned. However, their β -carotene hydroxylase gene is an obvious equivalent of the gene claimed in the instant invention.

Cunningham et al. do not teach that their “suitable promoter” is a glyceraldehyde-3-dehydrogenase promoter. Also, Cunningham et al. do not teach that their “recombinant yeast host organism” is *Phaffia rhodozyma*.

Anazawa et al. teach transformation of the filamentous fungi, *Monascus*, with a glyceraldehyde-3-dehydrogenase promoter. Anazawa et al. further describe this promoter as a “strong promoter.” Therefore, a skilled artisan would conclude that the glyceraldehyde-3-dehydrogenase promoter would be an obviously suitable promoter to express proteins in the filamentous fungi (yeast), *Phaffia rhodozyma*.

Van Ooyen et al. teach transformed *Phaffia rhodozyma* capable of producing carotenoids, including zeaxanthin (col.2, line 50) through introduction of plasmid comprising a suitable gene, “crtZ”(col.5, line 62-63) into *Phaffia rhodozyma*. The

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applicant will be familiar with the fact that “crtZ” is the name of the gene that encodes β -carotene hydroxylase. Van Ooyen et al. teach that the transformed *Phaffia* “is cultivated under conditions...the range of 15°-26°C. The preferred range is 20°-22°C.” (col.6, line 24). Van Ooyen et al. teach “the fermentation is performed in a medium...under aerobic conditions” (col.6, lines 25 & 30). While the exact length of time Van Ooyen et al. ferments their transformed *Phaffia rhodozyma* is not explicitly stated, a skilled artisan would understand that it falls within the range indicated in claim 8.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to produce zeaxanthin and β -cryptoxanthin from recombinant *Phaffia* that expresses a β -carotene hydroxylase gene.

The person of ordinary skill in the art would have been motivated to make that modification because, “Through cloning and expression of genes involved in the carotenoid biosynthetic pathway it also becomes possible to use *Phaffia rhodozyma* for obtaining desired carotenoids. Desired carotenoid production includes increased production of... carotenoids such as zeaxanthin,” (Van Ooyen, page 4, lines 1-6) and Cunningham et al. seek “method for augmenting the accumulation of carotenoids and production of novel and rare carotenoids. The present invention provides methods for controlling the ratio of various carotenoids in a host.” (Cunningham et al., col. 1, lines 11-15). Furthermore, Anazawa et al. indicate a suitable promoter for expression of proteins in fungi.

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An artisan would have expected success, because transformation of genes into Phaffia is a well understood technology.

Therefore the method as taught by Cunningham et al. in view Anazawa et al. and further in view of Van Ooyen in would have been *prima facie* obvious over the method of the instant application.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SDL/ Scott Long Patent Examiner, Art Unit 1633	/Janet L. Epps-Ford/ Primary Examiner, Art Unit 1633
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